REMARKS

I. Status Summary

Claims 1-12 and 45-54 are pending and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office"). Claims 1-12 and 45-54 presently stand rejected.

Claims 1-12 and 45-54 have been rejected under the enablement provision of 35 U.S.C. § 112, first paragraph.

Claims 1-12 and 45-54 have been rejected under 35 U.S.C. § 112, second paragraph upon several bases.

Claims 1-2, 4-7, 11-12, 45-46, and 48-51 have been rejected under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Kunzelmann-Marche *et al.* (2001) 276 *J Biol Chem* 5134-5139 (hereinafter "Kunzelmann-Marche") in view of U.S. Patent Application Publication No. 2002/0165353 of Malouf *et al.* (hereinafter "Malouf").

Claims 1, 5, 7, 11, 12, and 49 have been amended. Support for the amendments to the claims can be found throughout the specification as filed, including particularly at page 70, lines 18-32, page 80, lines 3-11, and page 81, lines 9-12 and 28-30 (claim 1). Additional support can be found at page 110, line 20 (claims 5 and 49); in the Examples (claim 7); at page 70, lines 25-27, and page 85, lines 32-33 (claims 11 and 12). Thus, no new matter has been added by the amendments to the claims.

Reconsideration of the application as amended and in view of the following remarks is respectfully requested.

II. Response to the Rejection under 35 U.S.C. § 112, First Paragraph

The Patent Office has rejected claims 1-12 and 45-54 under 35 U.S.C. § 112, first paragraph, upon the contention that the claims are not enabled. Specifically, the Patent Office contends that the test sample in the instant claims does not require that the platelet VDCC polypeptide be present in a cell membrane, nor does it require that cellular constituents required for phosphatidylserine (hereinafter "PS") exposure on the surface of the cell be present. The Patent Office further contends that without these cellular constituents, step (c) of claim 1 would not measure anything.

After careful consideration of the Patent Office's rejection and the basis therefore, Applicants respectfully traverse the rejection and submit the following remarks.

Applicants respectfully submit that the Patent Office appears to be asserting that the method of claim 1 requires the presence of a cell in order to provide a measurement in step (c). Applicants respectfully disagree. Applicants respectfully submit that the presently claimed method does not require the presence of a cell.

To elaborate, instant claim 1 provides a method for screening candidate substances for an ability to modulate PS exposure on the surface of a platelet by testing a candidate substance's effect on the biological activity of the VDCCα_1 subunit. Thus, the presently disclosed method screens candidate substances for an ability to increase or decrease a VDCCα_1 biological activity. While it is consistent with certain embodiments of the presently disclosed methods to provide a test sample that comprises a cell, since a biological activity of a VDCCα_1 subunit can be assayed in a cell free system (see page 71, lines 12-23 of the instant specification), the presence of an intact cell is not required to practice the method of claim 1. Furthermore, applicants respectfully submit that modulators that are found to effect a VDCCα_1 biological activity in a test sample can also be candidates for modulating phosphatidylserine (PS) exposure on the surface of a platelet.

Therefore, upon a review of the instant disclosure one of ordinary skill in the art would have appreciated that modulators of biological activities of the VDCCα_1 subunit disclosed in the instant application can be associated with PS exposure on the surface of a platelet. As such, consideration of the instant specification provides one of ordinary skill in the art with the ability to practice the methods of claims 1 and 45 without undue experimentation.

Accordingly, applicants respectfully submit that the instant specification fully enables claims 1 and 45. Furthermore, applicants respectfully submit that claims 2-12 and 46-54 all depend directly or indirectly from claim 1 or claim 45, respectively, and thus claims 2-12 and 46-54 are also believed to be enabled. As such, applicants respectfully request that the instant rejection of claims 1-12 and 45-54 under the first paragraph of 35 U.S.C. § 112 be withdrawn at this time.

III. Responses to the Rejections under 35 U.S.C. § 112, Second Paragraph

Claims 1-12 and 45-54 have also been rejected on several bases under the second paragraph of 35 U.S.C. § 112. Specifically, the Patent Office contends that claims 1, 3, 6, 7, 11, 12, 45, 47, and 50 are indefinite.

After careful consideration of the Patent Office's rejections and the reasons therefore, Applicants respectfully traverse the rejection and offer the following remarks.

III.A. Response to the Rejection of Claims 1 and 45

The Patent Office first asserts that claims 1 and 45 are confusing because the test sample is not required to have a cell where phosphatidylserine could be exposed. Applicants respectfully disagree that this could render the metes and bounds of the claims unclear. Particularly, applicants respectfully submit that upon consideration of the specification, one of ordinary skill in the art would understand the metes and bound of the claimed methods, and thus the claims fully comply with the requirements of 35 U.S.C. § 112, second paragraph, as set forth in the Court of Appeals for the Federal Circuit's opinion in Phillips V. AWH Corp., 415 F.3d 1303, 75 U.S.P.Q.2d 1321 (Fed. Cir. 2005).

To elaborate, applicants respectfully submit that as described hereinabove, a cell is not a required element of the test sample in the instantly claimed methods. The instant methods relate to screening candidate substances for an ability to modulate a biological activity of a VDCCα_1 subunit polypeptide. This can serve as a proxy for an ability to modulate PS exposure on surface of a platelet. As one of ordinary skill in the art would understand how to determine an effect on a biological activity of a VDCCα_1 subunit polypeptide without employing a test sample comprising a cell (*see* page 71, lines 12-23, of the instant specification) upon a review of the instant disclosure, applicants respectfully submit that one of ordinary skill of the art, when viewing the claims in light of the specification, would understand that a cell was not needed to practice the instant methods.

As such, applicants believe that the Patent Office's apparent assertion that it is unclear how the metes and bounds of claims 1 and 45 can be determined without a specific recitation of the test sample comprising a cell is inconsistent with the express

disclosure of the instant specification. Therefore, applicants respectfully submit that the instant rejection is improper, and respectfully request that it be withdrawn at this time.

III.B. Response to the Rejection of Claims 3 and 47

Next, the Patent Office asserts that claims 3 and 47 are confusing because the limitations set forth therein do not further modify the methods of claims 1 and 45. According to the Patent Office, the step of isolating a gene encoding the candidate polypeptide does not further limit the method of screening candidate substances for their ability to modulate phosphatidylserine on the surface of a cell. Additionally, the Patent Office asserts that not all of the candidate substances embraced by claims 2 and 46 would have a gene associated with them.

Turning first to the aspect of the Patent Office's rejection that is based on not all of the candidate substances embraced by claims 2 and 46 having a gene associated with them, applicants respectfully submit that while some embodiments of the subject matter of claims 2 and 46 might not have a gene associated with them, this does not support that claims 3 and 47 are indefinite. Applicants respectfully submit that the proper framework for considering whether a claim complies with the second paragraph of 35 U.S.C. § 112, second paragraph, is whether one of ordinary skill in the art would understand the meaning of the claim after consideration of the specification. Since claims 3 and 47 depend from claims 2 and 46, respectively, and claims 2 and 46 recite embodiments pertaining to candidate polypeptides, applicants respectfully submit that one of ordinary skill in the art would understand what the recitation in claims 3 and 47 to "isolating a gene encoding the candidate polypeptide" would encompass.

Furthermore, applicants respectfully submit that the assertion that the isolating step recited in claims 3 and 47 does not further limit the method of screening does not support a rejection under 35 U.S.C. § 112, second paragraph. Applicants respectfully submit that isolating a gene that encodes a candidate polypeptide would be understood by one of ordinary skill in the art in that, for example, the effect of the candidate polypeptide on the claimed VDCCα_1 biological activity could be confirmed by employing the isolated gene to produce a recombinant version of the candidate polypeptide.

Since it is clearly contemplated in the instant specification to employ libraries of candidates (*see e.g.*, Specification at page 71, lines 24-32), one of ordinary skill in the

art would understand how the step recited in claims 3 and 47 could be employed in the methods of claims 2 and 46. Accordingly, applicants respectfully submit that claims 3 and 47 fully comply with the requirements of 35 U.S.C. § 112, second paragraph.

III.C. Response to the Rejection of Claims 6 and 50

With respect to claims 6 and 50, the Patent Office asserts that these claims are confusing because the limitations set forth therein do not further modify the methods of claims 5 and 49. Furthermore, the Patent Office asserts that a recombinant cell line suitable for use appears to be implicit in the recitation of a cell in cell culture found in claims 5 and 49.

Applicants respectfully disagree. With respect to the first assertion, applicants respectfully submit that it is axiomatic that not all dependent claims must limit the precise subject matter of the claims from which they depend. An example of such a claim is a product-by-process claim, wherein a product produced by a particular process is claimed in a form such as "A product produced by the method of claim 1". It is believed that these claims are acceptably under current U.S. patent practice.

The same situation is believed to be present with respect to instant claims 6 and 50. These claims recite recombinant cell lines suitable for use in the methods of claims 5 and 49, respectively. As such, the claims are directed to compositions, and thus need not further limit the methods recited in the claims, provided that they are suitable for use in those methods.

Turning now to the second basis for the instant rejection, applicants respectfully submit that the Patent Office's assertion that a recombinant cell line suitable for use appears to be implicit in the recitation of a cell in cell culture found in claims 5 and 49 is inaccurate. Applicants respectfully submit that one of ordinary skill in the art would understand that not all embodiments of the cells that are in culture as per claims 5 and 49 would have to be recombinant cell lines. For example, a cell in culture could be a platelet, which would already contain a platelet VDCCα_1 subunit polypeptide, and thus would not have to be made recombinant in order to express a platelet VDCCα_1 subunit polypeptide. However, other cell types could also be employed in the methods of claims 5 and 49, and if they did not express a platelet VDCCα_1 subunit polypeptide,

they could be transformed with an expression construct (*i.e.*, made recombinant) that encoded a platelet VDCCα_1 subunit polypeptide.

Accordingly, it is not believed to be necessary that all cells in cell culture as recited in claims 5 and 49 be recombinant, and thus applicants respectfully submit that claims 6 and 50 fully comply with the requirements of 35 U.S.C. § 112, second paragraph, with respect to this aspect of the instant rejection.

Summarily, applicants respectfully submit that the Patent Office has adopted an improper basis for rejecting claims 6 and 50 under 35 U.S.C. § 112, second paragraph, and further has not considered embodiments of claims 5 and 49 that do not require that the cells in culture be recombinant cell lines. As such, applicants respectfully submit that the instant rejection is improper, and respectfully request that it be withdrawn at this time.

III.D. Response to the Rejection of Claim 7

Claim 7 has been rejected under 35 U.S.C. § 112, second paragraph, upon the contention that the claims is confusing as it lacks antecedent basis in claim 1 for "a surface of the test sample". Applicants have amended claim 7 to recite a sample comprising a platelet, and the determining steps recite determining a level of PS exposure of a surface of the platelet. Applicants respectfully submit that platelets are understood to have surfaces upon which PS can be exposed, and thus believe that the amendments to claim 7 address the instant rejection under 35 U.S.C. § 112, second paragraph. Applicants respectfully request that the instant rejection be withdrawn at this time.

III.E. Response to the Rejection of Claims 11 and 12

Claims 11 and 12 have been rejected upon the contention that they appear to require foreknowledge of what the results of the method of claim 1 will be. Additionally, the Patent Office asserts that the claims do not make clear which candidate substances will provide an increase or decrease in phosphatidylserine exposure on the surface of the cell.

Applicants respectfully submit that the instant assertions do not support a rejection under 35 U.S.C. § 112, second paragraph. Particularly, applicants respectfully submit that claim 1, the claim from which claims 11 and 12 depend, recite *inter alia* a

method for screening candidate substances for an ability to modulate PS exposure on the surface of a platelet by measuring an effect of the candidate substance on a VDCCα_1 biological activity. Applicants further respectfully submit that the term "modulate" is defined in the specification as "an increase, decrease, preservation, maintenance, or other effect of any or all biological activities or properties of a platelet VDCC". *See* Specification at page 70, lines 25-27. As such, applicants respectfully submit that one of ordinary skill in the art would understand claim 1 to encompass a method of screening for candidate substances that in some embodiments increase or in some embodiments decrease a biological activity of a VDCCα_1 subunit polypeptide.

Against this framework, applicants respectfully submit that claim 11 recites the case wherein the candidate substance increases a biological activity of a VDCCα_1 subunit polypeptide. Given that this is one of the possible functions that the candidate substance can have within the scope of claim 1, applicants respectfully submit that contrary to the Patent Office's assertion, it is not required that applicants have foreknowledge of what the results of the method of claim 1. Rather, applicants respectfully submit that claim 11 recited a method in which the effect of the candidate substance on a biological activity of a VDCCα_1 subunit polypeptide that is assayed in an increase in biological activity of a VDCCα_1 subunit polypeptide. Similarly, claim 12 recites that the biological activity of a VDCCα_1 subunit polypeptide that is assayed is a decrease in a biological activity of a VDCCα_1 subunit polypeptide. Given that claims 11 and 12 recite different subsets of the possible effects that can occur in claim 1, each of these claims is believed to be a proper dependent claim.

Furthermore, applicants respectfully submit that the Patent Office's apparent requirement that the claims make clear which candidate substances will provide an increase or decrease in phosphatidylserine exposure on the surface of the cell is unreasonable as the method of claim 1 is a screening method in which candidate substances that have these activities are identified. Applicants respectfully submit that in order to comply with 35 U.S.C. § 112, second paragraph, claims 11 and 12 must inform the skilled artisan of the metes and bounds of the claims. Since one of ordinary skill in the art after consideration of the specification would understand that the

screening methods of claims 11 and 12 are directed to screening for candidate substances that increase or decrease, respectively, a biological activity of a VDCCα_1 subunit polypeptide, applicants respectfully submit that claims 11 and 12 comply with 35 U.S.C. § 112, second paragraph.

Accordingly, applicants respectfully request that the instant rejection be withdrawn at this time. Applicants further respectfully submit that each of the rejections under 35 U.S.C. § 112, second paragraph, have been addressed, and that the claims are in condition for allowance. A Notice of Allowance to that effect is respectfully solicited.

IV. Response to the Rejection under 35 U.S.C. § 103(a)

The Patent Office has rejected claims 1-12 and 45-54 under 35 U.S.C. § 103(a) upon the contention that the claims are unpatentable over Kunzelmann-Marche *et al.* in view of Malouf. According to the Patent Office, Kunzelmann-Marche teaches screening candidate substances for their ability to modulate phophatidylserine exposure on the surface of a cell line that expresses receptors such as those found in platelets using flow cytometry. The reference is also asserted to disclose that Ca^{2+} channels in platelets would have been known to have been involved in phosphatidylserine exposure on the cell surface. The Patent Office concedes that the reference does not disclose the platelet voltage dependent calcium channel (VDCC) of SEQ ID NO: 2 that is encoded by the nucleic acid sequence of SEQ ID NO: 1, but asserts that this deficiency is cured by Malouf, which is asserted to disclose the platelet voltage dependent calcium channel (VDCC) of SEQ ID NO: 2 that is encoded by the nucleic acid sequence of SEQ ID NO: 1.

The Patent Office thus contends that it would have been obvious to screen candidate substances for their ability to modulate phophatidylserine exposure on the surface of a cell line where the VDCC taught by Malouf was present. The Patent Office further contends that one would have been motivated to do so as Malouf discloses that this VDCC is found in platelets and Kunzelmann-Marche teaches that calcium mobilization involving platelet calcium channels is involved in phosphatidylserine exposure on the surface of the cell.

After careful consideration of the Patent Office's rejection and the basis therefore, applicants respectfully traverse the rejection and submit the following remarks.

Initially, applicants respectfully submit that Malouf is the publication of the parent application to which the instant application claims priority. Therefore, applicants respectfully submit that any claims present in the instant application that are supported by the disclosure of the application that published as Malouf are entitled to the filing date of said application. Particularly, applicants respectfully submit that if the insant claims are entitled to the priority date of the Malouf publication, then by definition Malouf cannot be considered prior art. Applicants respectfully submit that the instant claims are fully entitled to the priority date of the application that published as Malouf because Malouf fully supports the instant claims.

To elaborate, Malouf provides for the screening of substances which modulate the biological activity of the VDCCα_1 subunit. *See* Malouf at paragraphs [0218]-[0230]. The instant claims also recite screening candidate substances to identify those which modulate the biological activity of VDCCα_1 subunit. Claim 45 recites a method of screening candidate substances for an ability to modulate platelet VDCCα_1 subunit biological activity. This method is disclosed in paragraph [0222] of Malouf.

In fact, claim 38 of U.S. Patent Application Serial No. 10/029,413 (*i.e.*, the application that published as Malouf) is identical to instant claim 45. As such, applicants respectfully submit that independent claim 45 is clearly entitled to the priority filing date of the parent application. Claims 46-54 either depend directly or indirectly on independent claim 45. Thus, dependent claims 46-54 are also entitled to the priority date of the parent application, and Malouf is not prior art with respect to claims 45-54.

Turning now to claim 1 and dependents thereof, applicants respectfully submit that these claims are also entitled to the priority date of U.S. Patent Application Serial No. 10/029,413. In paragraph [0230], the parent application discloses "a screening assay of the present invention can also involve determining the ability of a candidate substance to modulate...VDCCα_1 activity [and] thereby modulate the biological activity of calcium channels in target cells."

Therefore, applicants respectfully submit that the specification of U.S. Patent Application Serial No. 10/029,413 clearly supports the method recited in claims 1 and 45, and thus these claims are entitled to the priority date of U.S. Patent Application Serial No. 10/029,413. As a result, the effective filing date of claims 1-12 and 45-54 is the same as the effective date of Malouf as a reference, and thus applicants respectfully submit that Malouf is not available as art under 35 U.S.C. § 103(a).

Summarily, applicants respectfully submit that since the instant patent application is believed to have the same priority date as the parent application, the parent application cannot be properly considered prior art. Furthermore, since the Patent Office concedes that Kunzelmann-Marche does not teach or suggest every step of the instant claims (*see* Official Action at page 5), applicants further respectfully submit that Kunzelmann-Marche alone does not support a rejection of claims 1-12 and 45-54 under 35 U.S.C. § 103(a).

Accordingly, applicants respectfully request that the Patent Office withdraw the instant rejection of claims 1-12 and 45-54, and further respectfully solicits a Notice of Allowance for these claims.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

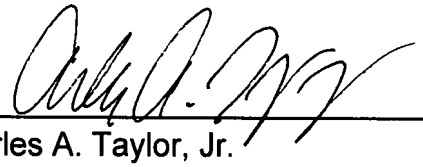
If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account No. **50-0426**.

Respectfully submitted,

JENKINS, WILSON, TAYLOR, & HUNT, P.A.

Date: July 24, 2007 By: 

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